Trichloroethylene

CAS #79-01-6
Swiss CD-1 mice, at 0.0, 0.15, 0.30, and 0.60% in feed
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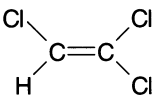
Started 7/3/84; Completed 2/25/86
NTIS #PB86173150/AS



Trichloroethylene (TCE), a common industrial solvent and dry cleaning agent, was tested for its effects on reproduction and fertility in Swiss CD-1 mice using the RACB protocol (Morrissey et al., Fundam Appl Toxicol 13:747–777 [1989]). TCE was microencapsulated in a gelatin and sorbitol shell and added to the diet. Data from a 2-week dose-range-finding study (Task 1) were used to set exposure concentrations for the Task 2 continuous cohabitation study at 0.15, 0.30, and 0.60% weight per weight. Based on the results of the analysis of feed formulations and an average daily feed consumption of approximately 5.0 g, the daily TCE dosages were approximately 100, 300, and 700 mg/kg/day.

TCE exposure was associated with no adverse clinical signs, and postpartum dam weights during the Task 2 cohabitation phase were not reduced by TCE. The only adverse reproductive change noted during Task 2 was a 4% reduction in pup weight adjusted for litter size at the high dose.

The last litter from the control and high dose groups was reared to weaning, for subsequent evaluation of second generation fertility. Maternal TCE exposure during lactation was associated with a significant increase in perinatal mortality: the 28% mortality rate in control litters is significantly less than the 61% mortality rats in the high dose TCE group. After weaning, mortality rates were comparable between the two groups.

After the F_1 pups were weaned, the F_0 control and high dose mice were killed and necropsied. Male body weight was not changed, while absolute testis weight was reduced by 4%, adjusted liver weight was increased by approximately 34%, and adjusted prostate weight was reduced by approximately 16%. Sperm motility was reduced by approximately 45% in the high dose TCE-treated animals; no other sperm or reproductive changes were noted. In females, body weight was unchanged while adjusted liver weight was increased by approximately 30%. No histologically visible changes in vaginal epithelium were noted. Treated mice had a greater incidence of centrilobular hypertrophy, and renal tubular degeneration and corticomedullary epithelial karyomegaly. Males were generally more affected than females.

The second generation mice from the control and high dose groups were cohabited at approximately postnatal day 74. No reproductive end point was altered by TCE exposure. After evaluation of the F_2 pups, the F_1 adults were killed and necropsied. Male body weight was unchanged, but adjusted liver weight was increased by approximately 60%, adjusted kidney weight was increased by approximately 9%, and adjusted epididymis weight increased by approximately 9%. The percent motile sperm was reduced by approximately 20%, while the proportion of abnormal sperm was increased from a control value of 8 to 10% in the treated mice. TCE-treated female body weights were not different from controls, while adjusted liver weight and kidney weight were increased by approximately 30 and 16%, respectively. Hepatic and renal microscopic lesions were similar to those noted for the F_0 mice. Histologic evaluation of the vaginal epithelium indicated cycling in both groups, but cycles were not assessed in vivo.

In summary, trichloroethylene exposure to mice via the diet produced significant hepatic and renal toxicity (increased weights and microscopic lesions), reduced sperm motility in both generations, and produced greater lactational mortality in the high dose group. These data suggest that the hepatic, renal, and lactational toxicities were more severe than the relatively moderate reductions in sperm motility.

Summary: NTP Reproductive Assessment by Continuous Breeding Study.

NTIS#: **PB86173150/AS**
Chemical: **Trichloroethylene**
CAS#: **79-01-6**
Mode of exposure: **Feed, microencapsulation**
Species/strain: **Swiss CD-1 mice**

F_0 generation — Dose concentration →	0.15%	0.30%	0.60%
General toxicity	Male, female	Male, female	Male, female
Body weight	—, —	—, —	—, —
Kidney weight[a]	•	•	—, —
Liver weight[a]	•	•	↑, ↑
Mortality	—, —	—, —	—, —
Feed consumption	—, —	—, —	—, —
Water consumption	•	•	•
Clinical signs	—, —	—, —	—, —
Reproductive toxicity			
x̄ litters/pair	—	—	—
# live pups/litter; pup wt./litter	—, —	—, —	—, ↓
Cumulative days to litter	—	—	—
Absolute testis, epididymis weight[a]	•	•	↓, —
Sex accessory gland weight[a] (prostate, seminal vesicle)	•	•	↓, —
Epidid. sperm parameters (#, motility, morphology)	•	•	—, ↓, —
Estrous cycle length	•	•	•

Determination of affected sex (crossover)	Male	Female	Both
Dose level	•	•	•

F_1 generation — Dose concentration →	0.15%	0.30%	0.60%
General toxicity	Male, female	Male, female	Male, female
Pup growth to weaning	•	•	—, —
Mortality	•	•	↑, ↑
Adult body weight	•	•	—, —
Kidney weight[a]	•	•	↑, ↑
Liver weight[a]	•	•	↑, ↑
Feed consumption	•	•	—, —
Water consumption	•	•	•
Clinical signs	—, —	—, —	—, —
Reproductive toxicity			
Fertility index	•	•	—
# live pups/litter; pup wt./litter	•	•	—, —
Absolute testis, epididymis weight[a]	•	•	—, ↑
Sex accessory gland weight[a] (prostate, seminal vesicle)	•	•	—, —
Epidid. sperm parameters (#, motility, morphology)	•	•	—, ↓, ↑
Estrous cycle length	•	•	•

Summary information	
Affected sex?	**Unclear**
Study confounders:	**None**
NOAEL reproductive toxicity:	**Not clear**
NOAEL general toxicity:	**Not clear**
F_1 more sensitive than F_0?	**No**
Postnatal toxicity:	**Yes**

Legend: —, no change; •, no observation; ↑ or ↓, statistically significant change ($p<0.05$); —, —, no change in males or females. [a]Adjusted for body weight.